Meta-analysis: the detection of pancreatic malignancy with positron emission tomography

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CRD summary
This review investigated the accuracy of fluorodeoxyglucose positron emission tomography (FDG-PET) as an adjunct to computed tomography for detecting pancreatic malignancy. The authors concluded that FDG-PET may enhance diagnosis, but its usefulness depends on the population group. The conclusion follows from the evidence presented; however, estimates of diagnostic accuracy may be imprecise due to methodological limitations in the available studies.

Authors’ objectives
To investigate the diagnostic accuracy of fluorodeoxyglucose positron emission tomography (FDG-PET) plus computed tomography (CT) compared with CT alone for the detection of pancreatic malignancy.

Searching
MEDLINE was searched up to April 2003 for studies published in the English language; the search terms were reported. The bibliographies of review articles were screened and some experts were contacted.

Study selection
Study designs of evaluations included in the review
Studies of at least 12 participants were eligible for inclusion.

Specific interventions included in the review
Studies evaluating the performance of FDG-PET as an adjunct to CT were eligible for inclusion. Direct comparisons of FDG-PET plus CT versus CT alone were not available.

Reference standard test against which the new test was compared
Studies were required to use a reference standard for the detection of malignancy to be included in the review, though the standard itself was not specified. The included studies used pancreatic biopsy or long-term follow-up of patients as the reference standard.

Participants included in the review
Studies of individuals undergoing assessment for pancreatic malignancy were eligible for inclusion. The included studies were of patients with clinical symptoms, with suspected cancer, with a mass on prior imaging, or who had been referred to a surgical centre for resection of a mass. The prevalence of pancreatic carcinoma ranged from 27 to 87%. The included participants had a positive, negative or indeterminate diagnosis for pancreatic cancer based on CT.

Outcomes assessed in the review
Inclusion criteria for the outcomes were not specified. The outcome measures used in the review were sensitivity and specificity.

How were decisions on the relevance of primary studies made?
Two reviewers independently screened studies and any disagreements were resolved by consensus.

Assessment of study quality
The following criteria were assessed: whether the sample was representative; clear description of the setting and patient selection; minimisation of differences between patients who received the tests; description of the scanner model; use of clearly defined criteria for test interpretation; use of clearly defined histopathological or clinical criteria for the confirmation of disease; and blinding of the test reader and person interpreting the reference standard. One point was given for the presence of each criterion and these were summed to give a total quality score.
At least two reviewers assessed the quality of each study and any discrepancies were resolved by consensus.

**Data extraction**
Two reviewers extracted the data and any disagreements were resolved by consensus. Data were extracted into predefined forms and 2x2 tables comparing the test results to the reference standard were generated. The sensitivity and specificity, with 95% confidence intervals (CIs), were calculated for each study.

**Methods of synthesis**
*How were the studies combined?*
When statistical homogeneity was present, a fixed-effect model was used to estimate a pooled sensitivity and specificity for FDG-PET and CT. The studies were weighted by sample size. A summary receiver operating characteristic curve was also generated. A funnel plot was used to detect the presence of publication bias.

*How were differences between studies investigated?*
The studies were pooled separately based on whether participants already had a positive diagnosis by CT, a negative CT or an indeterminate CT. An overall pooled estimate for FDG-PET as an adjunct to CT was planned only if these pooled sensitivities and specificities were similar. A pre-specified subgroup analysis was used to investigate the impact of quality, disease prevalence, reason for referral, results of previous imaging, study design and study location on the results. The chi-squared test and a Galbraith plot were used to investigate statistical heterogeneity.

**Results of the review**
Seventeen diagnostic accuracy studies (n=883) were included in the review.

All of the studies used a matched design to minimise differences between patients who received testing, described the scanner model, and defined clinical criteria for disease confirmation and test interpretation. However, none reported that the radiologist was blinded. There was generally a lack of clear recruitment procedures and poor descriptions of the study populations. No publication bias was detected.

Across all studies, the pooled sensitivity for CT was 81% (95% CI: 72, 88) and specificity was 66% (95% CI: 53, 77). Based on the pooling of 9 studies with appropriate data, the pooled sensitivity and specificity for PET were 92% (95% CI: 87, 95) and 68% (95% CI: 51, 81), respectively, in those with a positive CT, and 73% (95% CI: 50, 88) and 86% (95% CI: 75, 93) in those with a negative CT. In a single study, the sensitivity and specificity for PET were 100% and 68% in those with an indeterminate CT. Since there was a trend towards poorer test performance for FDG-PET in individuals with a negative CT, it was considered inappropriate to combine all these studies for an overall estimate for FDG-PET.

Based on the subgroup analysis, there were higher than average pooled estimates for studies with a lower quality score (3 studies) and for those who were referred for FDG-PET regardless of the results of conventional imaging (4 studies). There was no evidence of statistical heterogeneity.

**Authors’ conclusions**
Although the addition of FDG-PET to diagnostic work-up may enhance the diagnosis of pancreatic malignancy, there will be variation in its usefulness depending upon the pre-test probability of the patient, the results of the CT, and the provider's testing thresholds.

**CRD commentary**
The review addressed a clearly stated research question, though the inclusion criteria were very broad. The limited searches, combined with the restriction to English language publications, might have resulted in the loss of relevant data. Publication bias was assessed. The review methodology was well described and included measures to minimise the risk of error and bias. The methodological quality of the primary studies was assessed and their limitations were considered in the analysis, though an arbitrary cut-off for quality was used. Statistical and clinical heterogeneity was
investigated in the analysis. The authors' conclusions follow from the evidence presented, though the estimates of accuracy may be imprecise due to several methodological limitations in the available studies.

Implications of the review for practice and research
Practice: The authors stated that the benefit derived from the addition of PET to CT for the detection of pancreatic carcinoma depends upon the results of CT.

Research: The authors stated that a large prospective study is required to investigate the diagnostic accuracy and cost-effectiveness of FDG-PET as an adjunct to CT in populations with positive CT, negative CT and indeterminate CT.

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Other publications of related interest

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.